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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/646,493	08/21/2003	Eric Rose	50634-BA	9464
7590	09/28/2005			
John P. White Cooper & Dunham LLP 1185 Avenue of the Americas New York, NY 10036			EXAMINER RUSSEL, JEFFREY E	
			ART UNIT	PAPER NUMBER
			1654	

DATE MAILED: 09/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

10/646,493

Applicant(s)

ROSE ET AL.

Examiner

Jeffrey E. Russel

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 22 August 2005 and 25 April 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 9 and 38-44 is/are pending in the application.
- 4a) Of the above claim(s) 39-42 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 9 is/are rejected.
- 7) ☒ Claim(s) 38, 43 and 44 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 03 June 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)             | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

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1. Applicant's election with traverse of the species of Group 18 in the reply filed on August 22, 2005 is acknowledged. Applicants' arguments with respect to the rejoinder of the species of Groups 10 and 21 are convincing, and they have been re-joined and examined with the elected species.

With respect to the other species, the traversal is on the ground(s) that there would be no undue burden in examining all of the species. This is not found persuasive because as pointed out in the election of species requirement, the species are patentably distinct from one another, and the search of patentably distinct species would require multiple non-overlapping searches. This constitutes an undue burden upon the examiner.

The requirement is still deemed proper and is therefore made FINAL.

Claims 39-42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim.

Applicant timely traversed the restriction (election) requirement in the reply filed on August 22, 2005.

At page 8, last paragraph, of the response filed August 22, 2005, Applicants state that all pending claims embrace the elected species. However, it is not clear why claims 39-42 are said to embrace the elected species. None of these claims recite a mutation at position Ser185/Ser365.

2. The Sequence Listing filed August 22, 2005 is approved.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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4. Claim 9 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is no original disclosure supporting the recitation that the Factor IXa compound can be an anti-Factor IX antibody or fragment thereof, as is recited in claim 9(viii). The original disclosure is limited to antibodies or fragments thereof that bind to Factor IXa. See, e.g., page 9, lines 21-22, and originally-filed claims 14 and 16-18. Note that the current claim limitation embraces antibodies which bind to portions of Factor IX which are not present in Factor IXa, and thus the current claim limitation is broader in scope than the original disclosure.

5. Claim 9 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims recite a Factor IXa compound which is a small organic molecule or which is a peptidomimetic. The small organic molecules are defined almost entirely by function, and could literally embrace an uncountable number of small organic molecules. The peptidomimetics are defined almost entirely by function because the claims do not recite what particular peptides the peptidomimetics are supposed to mimic. There are no specific examples of small organic molecules or peptidomimetics described in the specification. The specification does not provide any guidance, theoretical basis for predicting or identifying, or method of obtaining compounds which might satisfy the claimed functional requirements. The absence of any specific examples

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and guidance does not demonstrate that Applicants had possession of the entire genus of claimed small organic molecules and peptidomimetics, and therefore Applicants can not be said to have provided an adequate written description of the claimed invention.

6. Claim 9 is rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for Factor IXa having a post-translational modification which is  $\gamma$ -carboxylation of glutamic acid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Colianni*, 195 USPQ 150 (CCPA 1977) and have been adopted by the Board of Patent Appeals and Interferences in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. With respect to (1), claim 9 recites a Factor IXa compound which is Factor IXa having a post-translational modification which is  $\gamma$ -carboxylation of glutamic acid. Factor IXa compounds are defined as being compounds which reduces or inhibits the conversion of Factor X to Factor Xa by naturally occurring Factor IX (see page 8, lines 26-28). With respect to (2), the WO Patent Application 95/17421 teaches that Factor IXa requires the presence of  $\gamma$ -carboxylated glutamic acid residues in order to be effective in converting Factor X to Factor Xa. See page 3, lines 28-35. With respect to (3), the relatively skill of those in the art is high. With respect to (4), the art involving

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coagulation via the intrinsic pathway is well understood and is relatively predictable. With respect to (5), the claim positively requires that  $\gamma$ -carboxylated glutamic acid residues be present in the Factor IXa. With respect to (6) and (7), the specification does not provide any direction or guidance as to how Factor IXa which retains its  $\gamma$ -carboxylated glutamic acid residues can be used to reduce or inhibit the conversion of Factor X to Factor Xa. No theory or proposed mechanism of action is disclosed which would explain why Factor IXa which retains its  $\gamma$ -carboxylated glutamic acid residues would exhibit the opposite of its expected activity, i.e. would not be able to convert Factor X to Factor Xa. There are no working examples in which Factor IXa which retains its  $\gamma$ -carboxylated glutamic acid residues is used to reduce or inhibit the conversion of Factor X to Factor Xa. With respect to (8), the quantity of experimentation necessary to be able to use Factor IXa which retains its  $\gamma$ -carboxylated glutamic acid residues to achieve the opposite of its natural function would be vast. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

7. Claim 9 is not deemed to be entitled under 35 U.S.C. 120 to the benefit of the filing date of parent application PCT/US97/08282 because the parent application, under the test of 35 U.S.C. 112, first paragraph, does not disclose anti-Factor IX antibodies or fragments thereof, does not disclose small organic molecules, and does not disclose peptidomimetics, for reasons analogous to those set forth in sections 5 and 6 above.

Claims 38, 43, and 44 are not deemed to be entitled under 35 U.S.C. 120 to the benefit of the filing date of parent applications PCT/US97/08282 or of U.S. application serial no.

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08/648,561 because the parent applications do not disclose the specific muteins recited in these claims.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claim 9 is rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent

Application 95/17421. The WO Patent Application '421 teaches peptide analogs of human factor IXa which compete with native factor IXa for binding to a platelet surface thereby inhibit factor IXa-induced activation of factor X. The peptide analogs are free of  $\gamma$ -carboxylated glutamic acid residues and have an artificially introduced restricted conformation, e.g., at least one cysteine-cysteine disulfide bond. See, e.g., the Abstract; page 13, lines 12-19; page 14, lines 4-6; Examples 2-4; and claims 1, 2, and 5. The peptide analogs of the WO Patent Application '421 therefore correspond to Applicants' inactive mutein form of Factor IXa.

10. Claim 9 is rejected under 35 U.S.C. 102(b) as being anticipated by the Larson et al article (J. Biol. Chem., Vol. 271, pages 3869-3876). The Larson et al article teaches a mutein of Factor IXa in which arginine occurs in place of glycine at position 12. The mutein is purified in Hepes-buffered saline, which corresponds to Applicants' pharmaceutically acceptable carrier. In the presence of activated factor VIIIa, the mutein will not augment cleavage of factor X. See, e.g.,

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the abstract; page 3871, column 1, second full paragraph; and page 3875, column 2, last paragraph.

11. Claim 9 is rejected under 35 U.S.C. 102(b) as being anticipated by Amparo et al (U.S. Patent No. 5,563,127). Amparo et al teach small organic molecules in the form of pharmaceutical compositions. The small organic molecules inhibit the activity of Factor IXa. See, e.g., column 319, lines 1-3, and claims 1, 6, and 7.

12. Claim 9 is rejected under 35 U.S.C. 102(e) as being anticipated by Blackburn et al (U.S. Patent No. 6,005,091). Blackburn et al teach monoclonal antibodies, designated BC1 and BC2, which bind to Factor IXa and which inhibit IXa activity. The antibodies are used to inhibit thrombosis. See, e.g., the Abstract; Figure 1; column 16, line 12 - column 17, line 37; and column 19, Table I.

13. Claims 38, 43, and 44 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The elected species, i.e. a pharmaceutical composition comprising an inactive mutein having a substitution at Ser185/Ser365 has been examined, and has been found to be novel and unobvious over the prior art of record or any combination thereof. Accordingly, the search has been extended to the other inactive muteins recited in instant claims 43 and 44, which have also been found to be novel and unobvious over the prior art of record.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

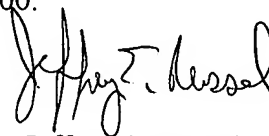


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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Bruce Campell can be reached at (571) 272-0974. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.



Jeffrey E. Russel

Primary Patent Examiner

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JRussel  
September 16, 2005